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HORMONAL COUNTERREGULATION DURING STANDARDIZED HYPOGLYCEMIA TEST COMPARING BIOSYNTHETIC HUMAN PROINSULIN AND HUMAN INSULIN

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The aim of this study was to compare the counterregulatory effects following administration of biosynthetic human proinsulin (BHPI) and human insulin (BHI) during hypoglycemia standardized by means of a glucose controlled insulin infusion system (GCIIS).

Material and methods: Eight healthy volunteers were studied after an overnight fast using the GCIIS (Biostator[®]) on static control as previously described (1).

Results: A total of 0.148±0.010 U/kg of BHPI had to be given by the GCIIS in order to obtain minimal blood glucose (BG) of 26±2 mg/dl (x±SEM) at 43±2 min. In contrast 0.083±0.004 U/kg of BHI were sufficient to produce a minimal BG of 21±1 mg/dl (n.s.) at 35±1 min (p<0.005).

Moreover, BHPI administration resulted in prolonged hypoglycemia and delayed BG recovery as compared to BHI (BG at 120 min: 46±3 for BHPI vs. 78±3 mg/dl for BHI). On a molar basis the BG lowering effect of BHPI was about 13% that of BHI. No severe side effects were observed and there was no need for dextrose administration, but clinical symptoms of hypoglycemia were more pronounced after BHPI infusion. Compared to BHI, BHPI produced higher peak levels for cortisol (252±16 vs. 168±10 ng/ml), a more pronounced secretion of GH and prolactin as well as a stronger decline of serum potassium (3.20±0.06 vs. 3.58±0.08 mmol/l). In addition, urinary epinephrine excretion following hypoglycemia after BHPI exceeded that after BHI (10.3±4.8 vs. 3.0±0.5 µg/120 min).

Conclusion: These preliminary results suggest that the observed more distinct glucose counterregulation is due to prolonged hypoglycemia rather than to any specific BHPI action on the hypothalamic-pituitary axis. Whether this "depot effect" may be beneficial in the treatment of diabetes mellitus remains to be established.

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